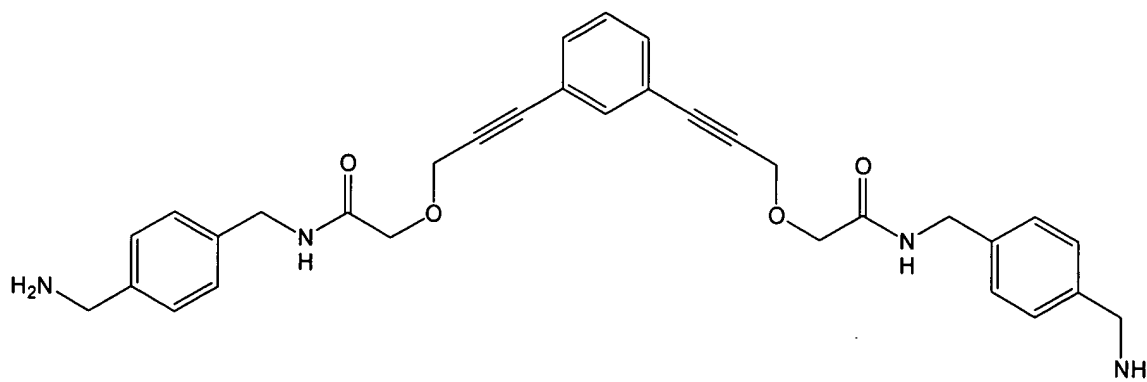


Applicant also submits that the Response filed on October 28, 2003 contained an inaccurate chemical structure of the provisionally elected species 1,3-Bis-(4-aminomethyl-benzylaminocarbonylmethyl-1-oxyprop-2-ynyl)-benzene. Applicant's attorney discussed this error with Examiner Tucker in a telephone conference February 2, 2004. The Examiner indicated that because no search has been conducted, the inaccurate structure provided would not impose an undue burden on the Examiner to re-search the presently claimed subject matter.

The correct chemical structure of 1,3-Bis-(4-aminomethyl-benzylaminocarbonylmethyl-1-oxyprop-2-ynyl)-benzene species is as follows:



1. Election / Restriction

The Official Action states the following, in relevant part:

[R]equirement for an election of species is proper in view of the fact that while the claimed compounds

might share a common property...compounds according to claim 1 do not possess a common structure—for at least the reasons that 6 distinct cores are specified in claim 1, and also because 5 distinct ring identities for A3 and A4 are possible (in addition to the acyclic alternatives for A3 and A4).

Additionally, in view of the multitudinous permitted identities for the B1, B2, A1, A2, B3, B4, A3, A4, B5, B6, A5, A6, K1, K2, X1, X2, Y1, Y2, Z1 and Z2, to suggest that every compound of claim 1 possesses a common structure would fly in the face of reason.

The election of 1,3-Bis-(4-aminomethyl-benzylaminocarbonylmethyl-1-oxyprop-2-ynyl)-benzene, which applicant states is readable on claims 1-4 and 6-8 is noted.

Claims 5, 9 and 10 therefore stand withdrawn with traverse, as not readable on the elected species.

RESPONSE

Applicant thanks the Examiner for his comments regarding the election of species. Applicant has filed herewith amendments to claims 1-3 and 6-8. In so doing, applicant has amended claim 1 to contain only one distinct core for the definition of "M", and have amended the definition of A3 and A4 to contain only one ring structure and several acyclic alternatives.

Applicant respectfully submits to the Examiner that amended claims 1-3 and 6-8 read on the elected species. Claims 9 and 10 also read on the elected species. Original claims 4 and 5 fall within the amended genus of claim 1.

Accordingly, applicant respectfully requests that the Examiner re-enter withdrawn claims 5, 9 and 10 and consider all claims presented herein for examination.

**2. Rejection of claims 1-4 and 6-8 due to Misjoinder of
Invention**

The Official Action states the following, in relevant part:

Claim 1 constitutes an improper joinder of inventions as it groups together species that are distinct and separately classified, and will support separate patents. The instant generic claim constitutes an improper joinder of inventions.

37 C.F.R. 1.104

(b) Completeness of Examiner's Action

The examiner's action will be complete as to all matters, except that in appropriate circumstances, such as misjoinder of invention, fundamental defects in the application, and the like, the action of the examiner may be limited to such matters before further action is made. However, matters of form need not be raised by the examiner until a claim is found allowable.

(c) Rejection of claims.

(1) If the invention is not considered patentable, or not considered patentable as claimed, the claims or those considered unpatentable will be rejected.

Thus, claim 1 is rejected because it is not deemed patentable by the Office at this time. Claims 2-4 and 6-8, which depend from claim 1 are also rejected because they depend from a rejected claim.

Applicant need provide a searchable genus, from the elected species.

RESPONSE

Applicant thanks the Examiner for his comments regarding providing a searchable genus. As stated above, applicant has filed herewith amendments to claims 1-3 and 6-8. Applicant respectfully submits that claim 1 contains a searchable genus as required by the Examiner.

As such, amended claims 1-3 and 6-8 read on the elected species. Claims 9 and 10 also read on the elected species. Original claims 4 and 5 fall within the amended genus of claim 1.

Accordingly, applicant respectfully requests that the Examiner re-enter withdrawn claims 5, 9 and 10 and consider all claims presented herein for examination.

CONCLUSION

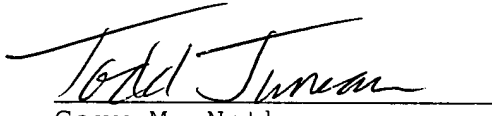
In view of the foregoing, applicant respectfully requests the Examiner to reconsider and withdraw the rejection of claims 1-4 and 6-8, re-enter withdrawn claims 5, 9 and 10, and to examine all of the claims pending in this application.

If the Examiner has any questions or wishes to discuss this matter, the Examiner is welcomed to telephone the undersigned attorney.

Respectfully submitted,

NATH & ASSOCIATES PLLC

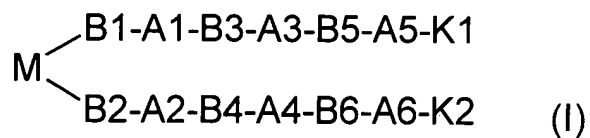
Date: February 5, 2004
NATH & ASSOCIATES PLLC
1030 Fifteenth Street, N.W.
Sixth Floor
Washington, D.C. 20005-1503
Telephone: (202) 775-8383
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Gary M. Nath
Reg. No. 26,965
Todd L. Juneau
Reg. No. 40,669
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Appendix A

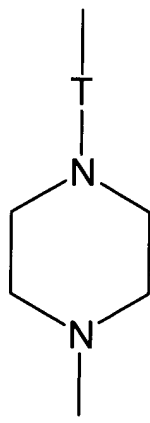
1. (Currently Amended) A compound ~~Compounds~~ of formula I



in which

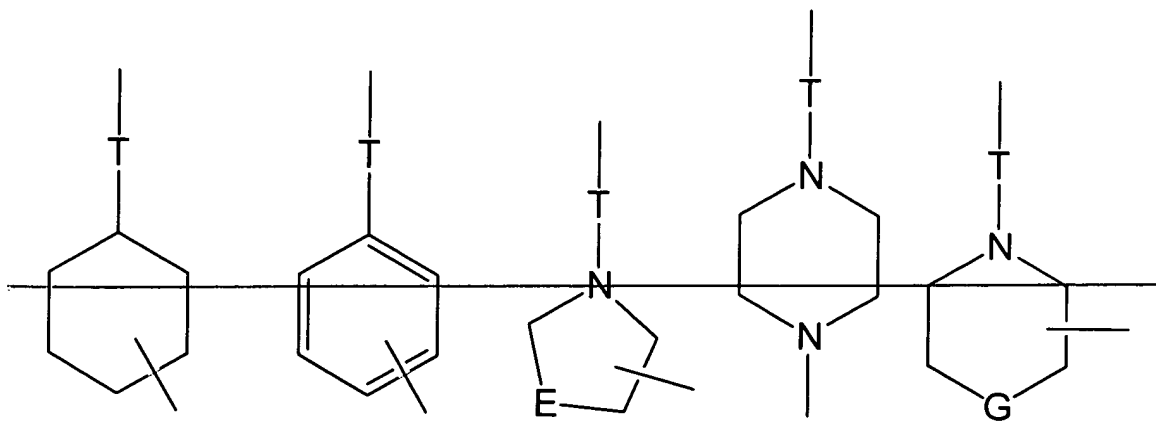
A1 and A2 are identical or different and are -C(O)-, -NH-,
 -O- (oxygen), -S- (sulfur), -S(O)₂-, -S(O)₂-NH-,
 -NH-S(O)₂-, -C(O)-NH-, -NH-C(O)-, -O-C(O)-, -C(O)-O-,
 or a bond,

A3 and A4 are identical or different and are -C(O)-, -O-,
 -S-, -NH-, -O-C(O)-, -C(O)-O-, -C(O)-NH-, -NH-C(O)-,



or a bond, or

~~are selected from the group consisting of~~



where

~~E is O (oxygen), S (sulfur) or CH₂ (methylene),~~

~~G is O (oxygen) or CH₂ (methylene),~~

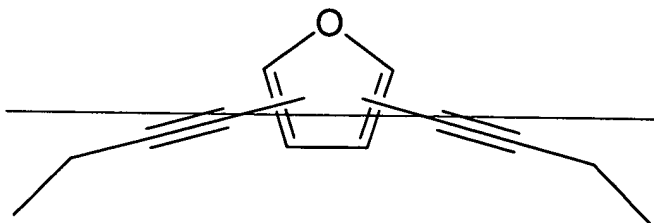
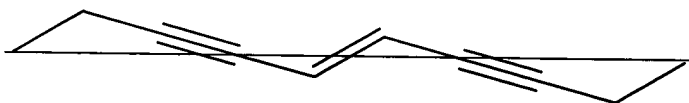
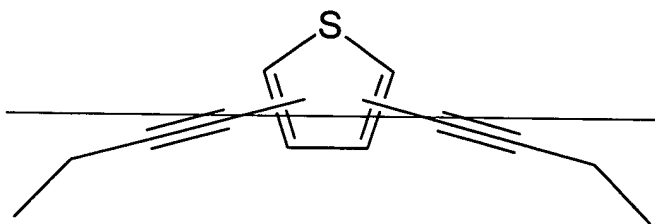
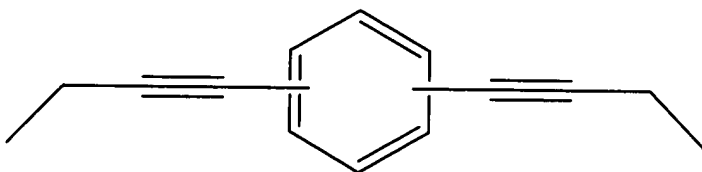
T is the group -C(O)- or a bond,

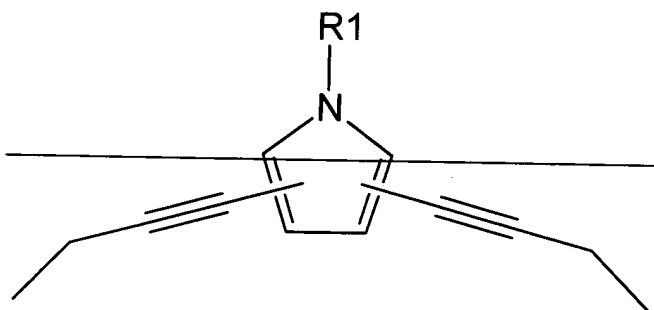
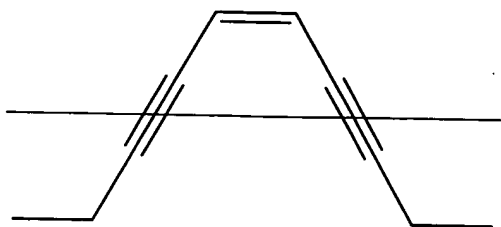
A5 and A6 are identical or different and are -C(O)-, -NH-,

-O-, -S-, -C(O)-NH-, -NH-C(O)-, -O-C(O)-, -C(O)-O-,

-NH-C(O)-NH- or a bond,

M is a the central building block ~~selected from the group~~
below





where

~~R1 is hydrogen, 1-4C-alkyl or 1-4C-alkylcarbonyl,~~

K1 is $-B7-(C(O))_m-B9-X1$, $-B7-(C(O))_m-B9-Y1$ or

$-B7-(C(O))_m-B9-Z1-B11-X1$,

K2 is $-B8-(C(O))_p-B10-X2$, $-B8-(C(O))_p-B10-Y2$ or

$-B8-(C(O))_p-B10-Z2-B12-X2$,

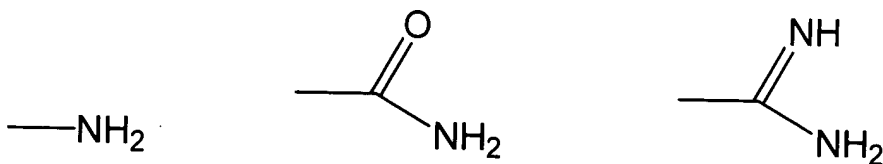
B1, B2, B3, B4, B5 and B6 are identical or different and
are a bond or 1-4C-alkylene,

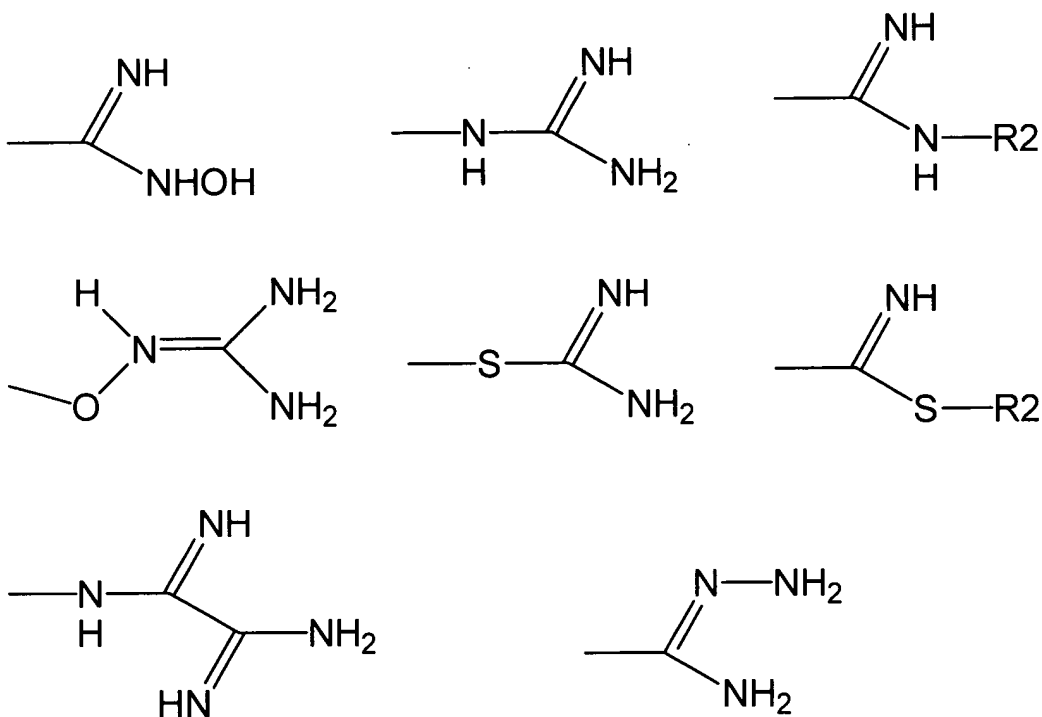
B7, B8, B9, B10, B11 and B12 are identical or different and
are a bond or 1-4C-alkylene,

m is 0 or 1,

p is 0 or 1,

X1 and X2 are identical or different and are selected from
the group consisting of





where

R₂ is 1-4C-alkyl,

Y₁ and Y₂ are identical or different and are a 4-11C-heteroaryl or 2-7C-heterocycloalkyl radical containing at least one ring nitrogen,

Z₁ and Z₂ are identical or different and are 5-12C-arylene, 5-12C-heteroarylene, 3-8C-cycloalkylene or 3-8C-heterocycloalkylene,

where each arylene, heteroarylene, cycloalkylene, heterocycloalkylene, heteroaryl or heterocycloalkyl may additionally for its part be substituted by one, two or three substituents selected from the group consisting of hydroxyl, halogen, nitro, cyano, amino, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, 1-4C-alkylcarbonyloxy, carboxyl or aminocarbonyl,

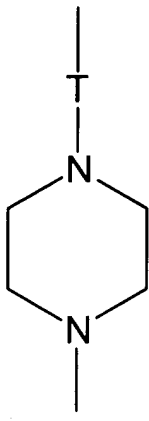
and

where on the direct route between the terminal nitrogen atoms 20 to 40 bonds have to be present, the salts of these compounds, and the N-oxides of the nitrogen-containing heteroaryls, heterocycloalkyls, heteroarylenes and heterocycloalkylenes, ~~and their salts,~~ or a salt, hydrate, hydrate of a salt, or solvate thereof, and ~~where all these wherein the~~ compounds are ~~excluded~~ in which one or more of the variables B1, B2, B3, B4, B5, B6, B7, B8, B9, B10, B11 or B12 may assume the meaning of a bond resulting in the direct linkage of two heteroatoms or two carbonyl groups are excluded.

2. (Currently amended) A compound ~~Compounds~~ of formula I according to claim 1 in which

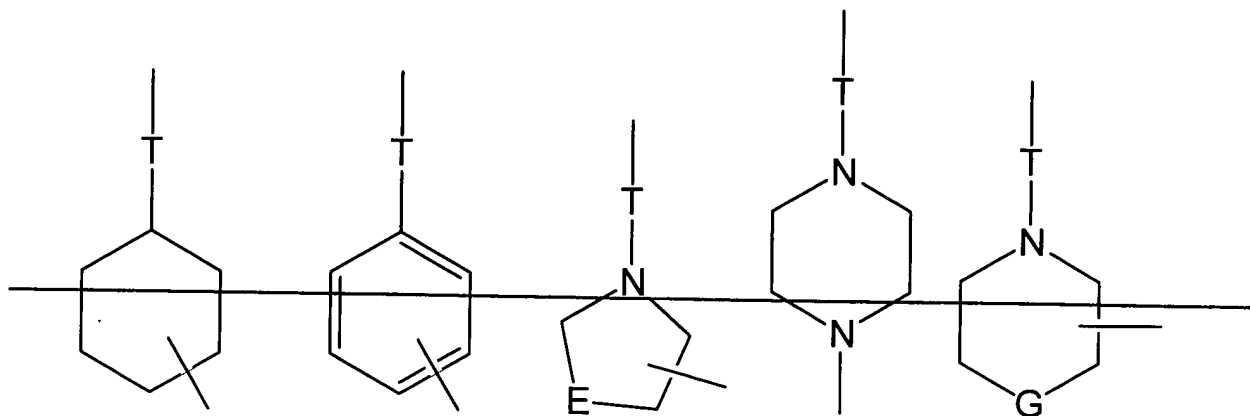
A1 and A2 are identical or different and are -C(O)-, -NH-, -O-, -C(O)-NH-, -NH-C(O)-, -O-C(O)-, -C(O)-O- or a bond,

A3 and A4 are identical or different and are -C(O)-, -O-, -NH-, -O-C(O)-, -C(O)-O-, -C(O)-NH-, -NH-C(O)-, or ~~or~~ a



bond, or

~~are selected from the group consisting of~~



where

~~E is O (oxygen), S (sulfur) or CH₂ (methylene), and~~

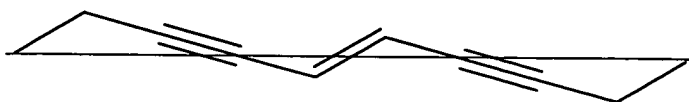
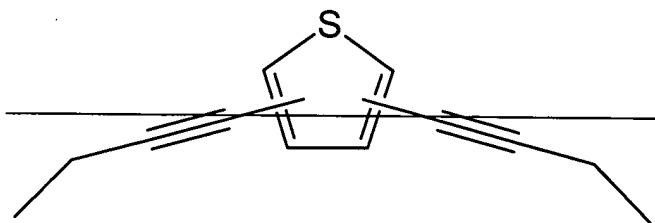
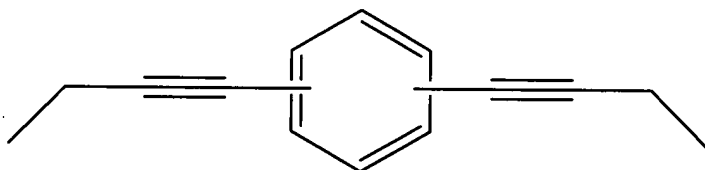
T is the group -C(O)- or a bond,

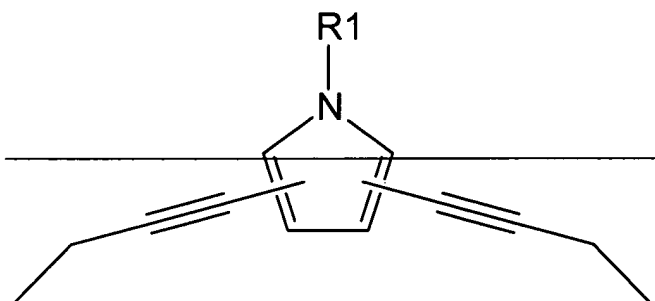
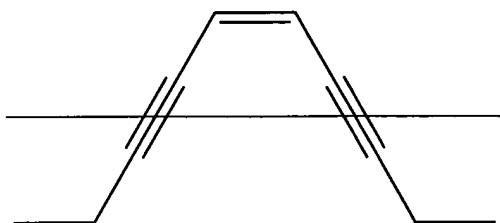
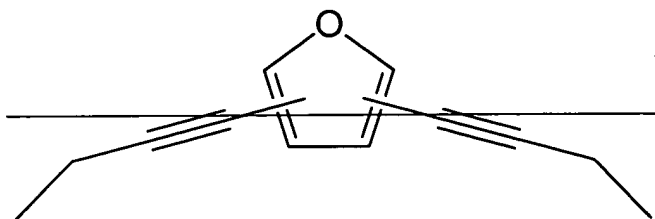
A5 and A6 are identical or different and are -C(O)-, -NH-,

-O-, -C(O)-NH-, -NH-C(O)-, -O-C(O)-, -C(O)-O-,

-NH-C(O)-NH- or a bond,

M is ~~a~~ the central building block ~~selected from the group~~
below





where

~~R1 is hydrogen, 1-4C alkyl or 1-4C alkylcarbonyl,~~

K1 is $-B7-(C(O))_m-B9-X1$, $-B7-(C(O))_m-B9-Y1$ or

$-B7-(C(O))_m-B9-Z1-B11-X1$,

K2 is $-B8-(C(O))_p-B10-X2$, $-B8-(C(O))_p-B10-Y2$ or

$-B8-(C(O))_p-B10-Z2-B12-X2$,

B1, B2, B3, B4, B5 and B6 are identical or different and

are a bond or 1-4C-alkylene,

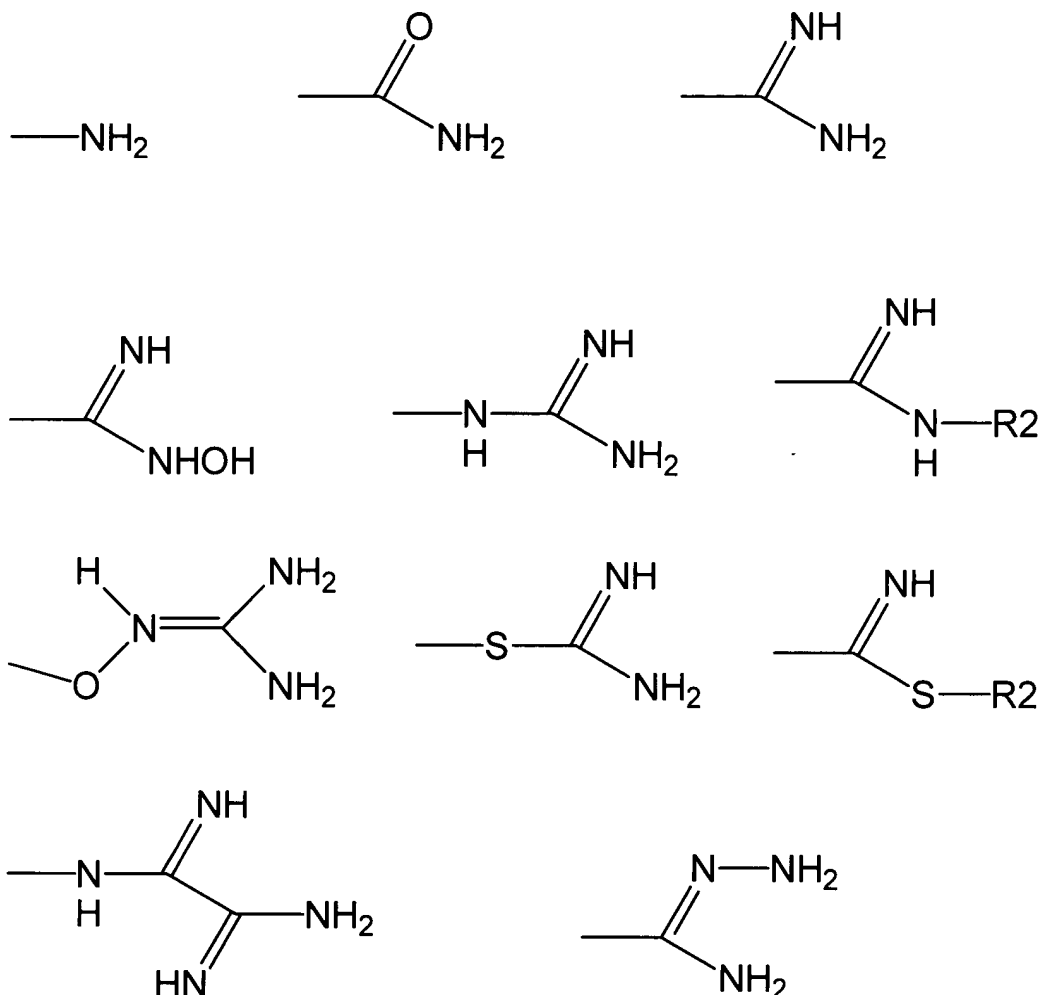
B7, B8, B9, B10, B11 and B12 are identical or different and

are a bond or 1-4C-alkylene,

m is 0 or 1,

p is 0 or 1,

X1 and X2 are identical or different and are selected from the group consisting of



where

R2 is 1-4C-alkyl,

Y1 and Y2 are identical or different and are piperid-4-yl, piperid-3-yl, piperazin-1-yl, piperazin-2-yl, morpholin-2-yl, pyrrolidin-2-yl, pyrrolidin-3-yl, imidazolidin-1-yl, imidazolidin-2-yl, imidazolidin-4-yl, 2-imidazolin-3-yl, 2-imidazolin-2-yl, imidazol-1-yl, imidazol-2-yl, imidazol-4-yl, pyrid-4-yl, pyrid-3-

yl, pyridazin-4-yl, pyrimidin-5-yl, pyrimidin-4-yl, indol-3-yl, benzimidazol-4-yl or benzimidazol-5-yl, Z1 and Z2 are identical or different and are 1,4-phenylene, 1,3-phenylene, 1,4-naphthylene, 2,6-naphthylene, 1,4-cyclohexylene, 1,3-cyclohexylene, 1,3-cyclopentylene, 1,4-piperazinylene, 4,1-piperadinylene, 1,4-piperadinylene, 2,5-pyrrolidinylene, 4,2-imidazolidinylene, 2,5-furylene, 2,5-pyrrolylene, 4,2-pyridylene, 5,2-pyridylene, 2,5-indolylene, 2,6-indolylene, 3,5-indolylene, 3,6-indolylene, 3,5-indazolylene, 3,6-indazolylene, 2,6-quinolinylene, 2,5-benzofuranylene or 4,2-thiozolylene, where each arylen, heteroarylen, cycloalkylene, heterocycloalkylene, heteroaryl or heterocycloalkyl may additionally for its part be substituted by one, two or three substituents selected from the group consisting of hydroxyl, halogen, nitro, cyano, amino, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, 1-4C-alkylcarbonyloxy, carboxyl or aminocarbonyl,

and

where on the direct route between the terminal nitrogen atoms 20 to 40 bonds have to be present, the salts of these compounds, and the N-oxides of the nitrogen-containing heteroaryls, heterocycloalkyls, heteroarylenes and heterocycloalkylenes, ~~and their salts,~~ or a salt, hydrate, hydrate of a salt, or solvate thereof, and

~~where all those wherein the~~ compounds ~~are excluded~~ in which one or more of the variables B1, B2, B3, B4, B5, B6, B7, B8, B9, B10, B11 or B12 may assume the meaning of a bond, resulting in the direct linkage of two heteroatoms or carbonyl groups are excluded.

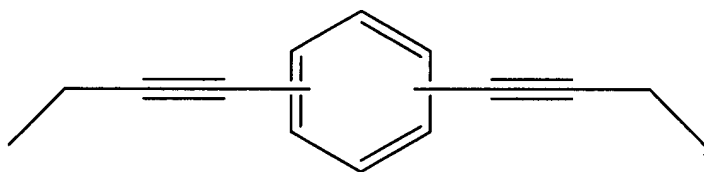
3. (Currently amended) A compound ~~Compounds~~ of formula I according to claim 1 in which

A1 and A2 are identical or different and are -O-, -C(O)-, -O-C(O)-, -NH-C(O)- or a bond,

A3 and A4 are identical or different and are 1,4-piperazinylene, ~~1,4-piperadinylene, 1,4-cyclohexylene, 1,3-phenylene~~ or a bond,

A5 and A6 are identical or different and are -C(O)-, -C(O)-NH-, -NH-C(O)- or -NH-C(O)-NH-,

M is a the central building block ~~selected from the group below~~



K1 is -B7-(C(O))_m-B9-Y1 or -B7-(C(O))_m-B9-Z1-B11-X1,

K2 is -B8-(C(O))_p-B10-Y2 or -B8-(C(O))_p-B10-Z2-B12-X2,

B1 and B2 are identical or different and are a bond or methylene,

B3, B4, B5 and B6 are identical or different and are a bond or 1-3C-alkylene,

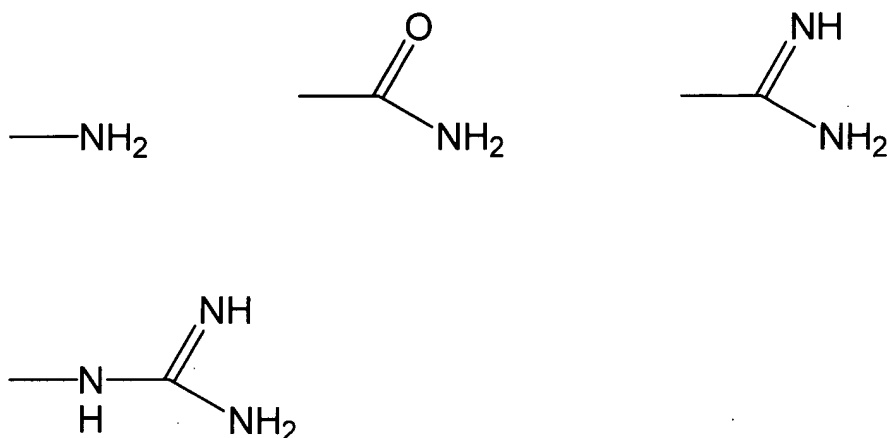
B7, B8, B9 and B10 are identical or different and are a bond or 1-4C-alkylene,

B11 and B12 are identical or different and are a bond or methylene,

m is 0,

p is 0,

X1 and X2 are identical or different and are selected from the groups below



Y1 and Y2 are imidizol-1-yl,

Z1 and Z2 are identical or different and are 5,2-

pyridinylene, 6-methyl-5,2-pyridinylene, 4,1-piperidinylene, 3,6-indazolylene, 3,6-indolylene, 1,3-phenylene, 1,4-phenylene, 1,3-cyclohexylene or 1,4-cyclohexylene,

and where on the direct route between the terminal nitrogen atoms 20 to 40 bonds have to be present, the salts of these compounds, and the N-oxides of the nitrogen-containing heteroaryls, heteroarylenes and heterocycloalkylenes, and their salts, or a salt, hydrate, hydrate of a salt, or solvate thereof,

~~where all those~~ wherein the compounds are ~~excluded~~ in which one or more of the variables B1, B2, B3, B4, B5, B6, B7, B8, B9, B10, B11 or B12 may assume the meaning of a bond resulting in the direct linkage of two heteroatoms or carbonyl groups are excluded.

4. (Original) A compound ~~Compounds~~ of formula I according to claim 1 in which

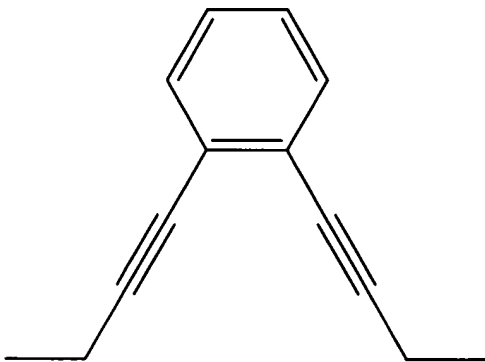
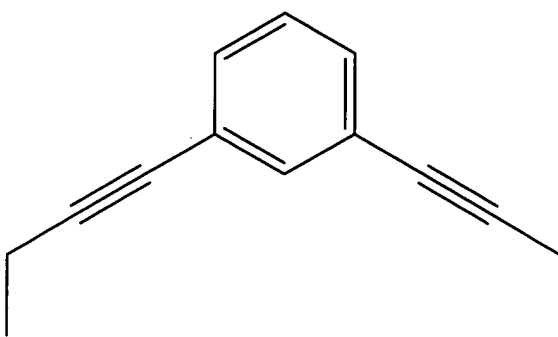
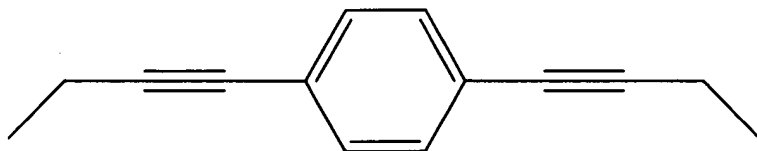
A1 and A2 are -O-C(O)-,

A3 and A4 are 1,4-piperazinylene,

A5 and A6 are identical or different and are $-C(O)-$ or

$-C(O)-NH-$,

M is a central building block selected from the groups below



K1 is $-B7-(C(O))_m-B9-Z1-B11-X1$,

K2 is $-B8-(C(O))_p-B10-Z2-B12-X2$,

B1, B2, B3, B4, B5 and B6 are a bond,

B7 and B8 are identical or different and are a bond or methylene,

B9 and B10 are a bond,

B11 and B12 are methylene,

m is 0,

p is 0,

X1 and X2 are amino,

Z1 and Z2 are identical or different and are 1,4-phenylene
or 1,4-cyclohexylene,

~~and the salts of these compounds~~ or a salt, hydrate,
hydrate of a salt, or solvate thereof.

5. (Original) A compound ~~Compounds~~ of formula I according
to claim 1 with the chemical name

1,2-bis[4-trans-4-aminomethylcyclohexylcarbonyl)-1-
piperazinylcarbonyl-1-oxyprop-2ynyl]benzene;

1,4-bis[4-trans-4-aminomethylcyclohexylcarbonyl)-1-
piperazinylcarbonyl-1-oxyprop-2ynyl]benzene;

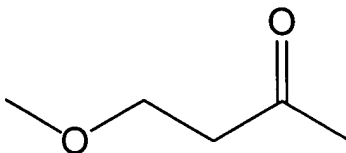
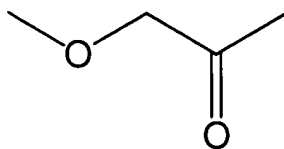
1,2-bis[4-(4-aminomethylbenzylaminocarbonyl)-1-
piperazinylcarbonyl-1-oxyprop-2ynyl]benzene;

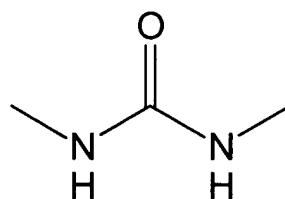
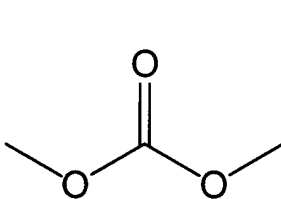
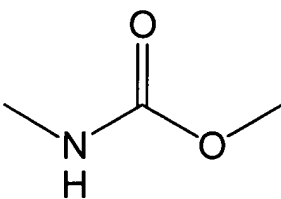
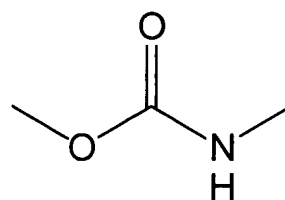
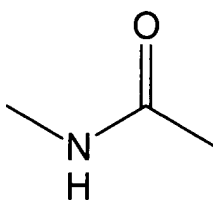
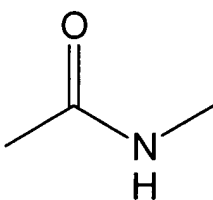
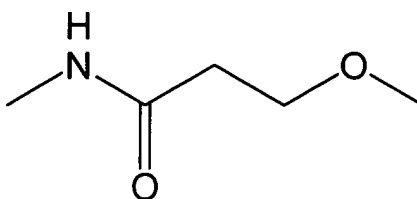
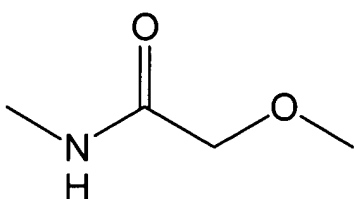
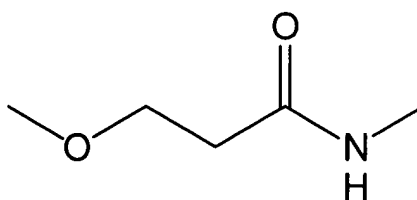
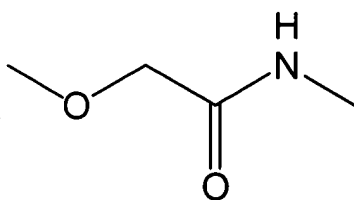
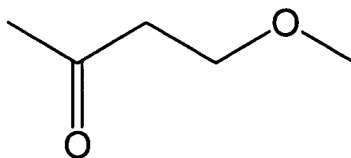
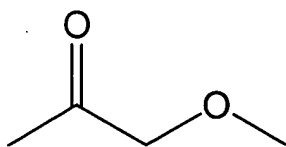
1,3-bis[4-(4-aminomethylbenzylaminocarbonyl)-1-
piperazinylcarbonyl-1-oxyprop-2ynyl]benzene;

~~and the salts of these compounds~~ or a salt, hydrate,
hydrate of a salt, or solvate thereof.

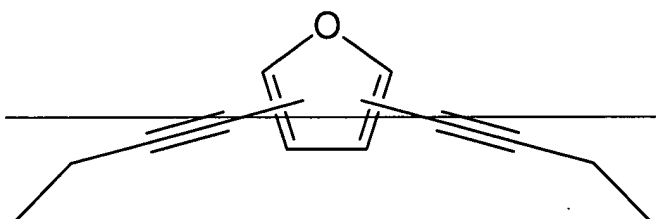
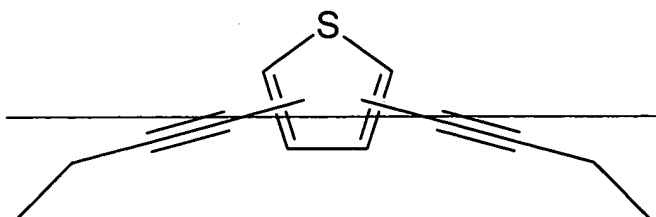
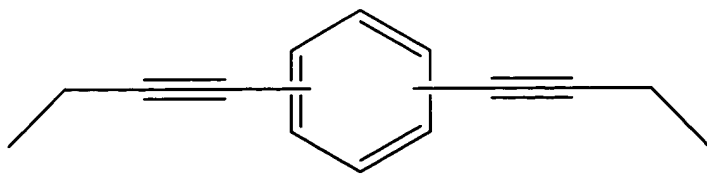
6. (Currently amended) A compound ~~Compounds~~ of formula I
according to claim 1 in which

-B1-A1-B3-A3-B5-A5- and -B2-A2-B4-A4-B6-A6- are identical
or different and are selected from the groups below





M is a the central building block ~~selected from the groups~~
below



K1 is $-B7-(C(O))_m-B9-Y1$ or $-B7-(C(O))_m-B9-Z1-B11-X1$,

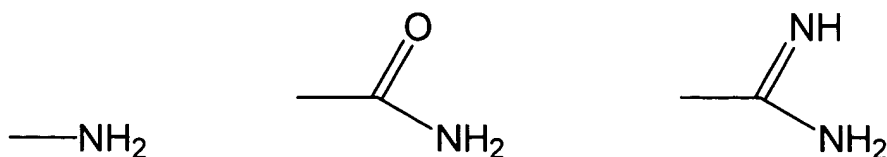
K2 is $-B8-(C(O))_p-B10-Y2$ or $-B8-(C(O))_p-B10-Z2-B12-X2$,

B7, B8, B9, B10, B11 and B12 are identical or different and
are a bond or 1-2C-alkylene,

m is 0,

p is 0,

X1 and X2 are identical or different and are selected from
the groups below



Y1 and Y2 are imidazol-1-yl,

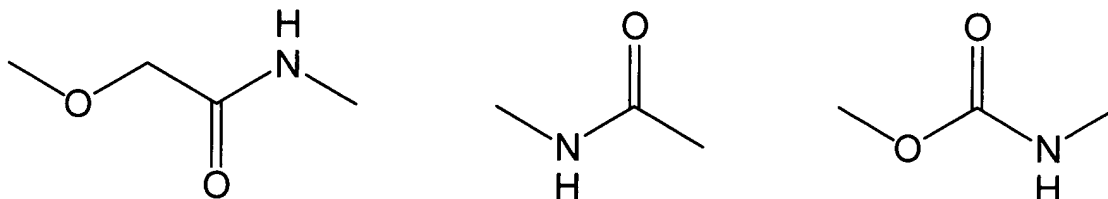
Z1 and Z2 are identical or different and are 5,2-

pyridinylene, 6-methyl-5,2-pyridinylene, 4,1-piperidinylene, 3,6-indazolylene, 3,6-indolylene, 1,3-phenylene, 1,4-phenylene, 1,3-cyclohexylene or 1,4-cyclohexylene,

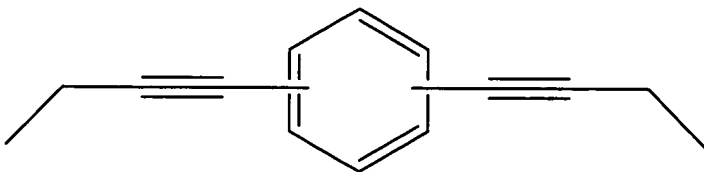
and where on the direct route between the terminal nitrogen atoms 20 to 33 bonds have to be present, the salts of these compounds, and also the N-oxides of the nitrogen-containing heteroaryls, heteroarylenes and heterocycloalkylenes, ~~and their salts~~ or a salt, hydrate, hydrate of a salt, or solvate thereof.

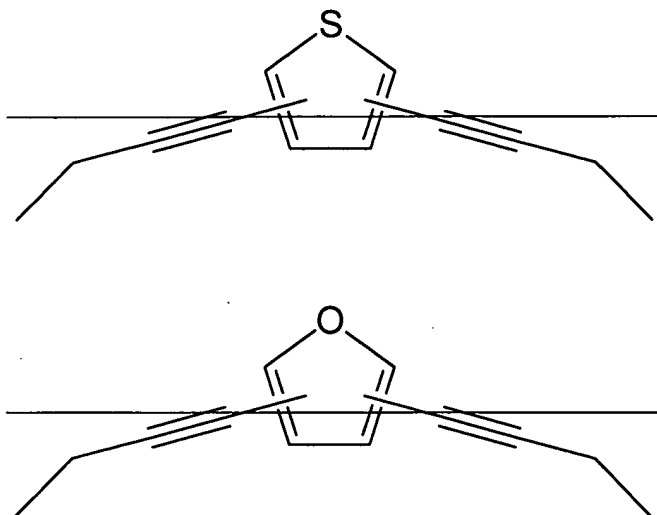
7. (Currently amended) A compound ~~Compounds~~ of formula I according to claim 1 in which

-B1-A1-B3-A3-B5-A5- and -B2-A2-B4-A4-B6-A6- are identical or different and are selected from



M is a the central building block ~~selected from the group~~ below





K1 is $-B7-(C(O))_m-B9-Z1-B11-X1$,

K2 is $-B8-(C(O))_p-B10-Z2-B12-X2$,

B7 and B8 are identical or different and are a bond or methylene,

B9 and B10 are a bond,

B11 and B12 are methylene,

m is 0,

p is 0,

X1 and X2 are amino,

Z1 and Z2 are identical or different and are 1,4-phenylene or 1,3-phenylene,

~~and the salts of these compounds~~ or a salt, hydrate, hydrate of a salt, or solvate thereof..

8. (Currently amended) A compound ~~Compounds~~ of formula I according to claim 1 with the chemical name

1,3-Bis-(4-aminomethylbenzylaminocarbonyl-1-oxyprop-2-ynyl)-benzene;

1,2-Bis-(4-aminomethylbenzylaminocarbonyl-1-oxyprop-2-ynyl)-benzene;

~~3,4-Bis-(4-aminomethylbenzylaminocarbonyl-1-oxyprop-2-ynyl)-thiophene;~~

~~2,5-Bis-(4-aminomethylbenzylaminocarbonyl-1-oxyprop-2-ynyl)-furan;~~

~~2,5-Bis-(3-aminomethylbenzylaminocarbonyl-1-oxyprop-2-ynyl)-furan;~~

~~3,4-Bis-(3-aminomethylbenzylaminocarbonyl-1-oxyprop-2-ynyl)-thiophene;~~

1,4-Bis-(4-aminomethylbenzylaminocarbonylmethyl-1-oxyprop-2-ynyl)-benzene;

1,3-Bis-(4-aminomethylbenzylaminocarbonylmethyl-1-oxyprop-2-ynyl)-benzene;

1,4-Bis-(4-aminomethylbenzylcarbonyl-1-aminoprop-2-ynyl)-benzene;

1,2-Bis-(4-aminomethylbenzylcarbonyl-1-aminoprop-2-ynyl)-benzene;

1,4-Bis-(4-aminomethylphenylethylcarbonyl-1-aminoprop-2-ynyl)-benzene;

~~and the salts of these compounds~~ or a salt, hydrate, hydrate of a salt, or solvate thereof.

9. (Currently amended) A pharmaceutical composition comprising ~~one or more compounds~~ a compound of formula I according to claim 1 ~~and~~ or a pharmaceutically acceptable salt, hydrate, hydrate of a salt or solvate thereof; and a suitable pharmaceutical excipient.

10. (Currently amended) A method of treating an airway disorder in a patient comprising administering to a patient in need thereof a therapeutically effective amount of ~~one or more compounds~~ a compound of ~~formula I~~ according to claim 1, or a pharmaceutically acceptable salt, hydrate, hydrate of a salt or solvate thereof.